IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Miri Seiberg, et al.

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Attorney Docket No.: JBP 518

Title: Soy Depigmenting and Skin Care Compositions

DECLARATION OF MIRI SEIBERG, PH.D.

I, Miri Seiberg, am a Distinguished Research Fellow in the Skin Research Center at Johnson & Johnson Consumer Companies, Inc. My education includes a Ph.D. in Molecular Biology from The Weizmann Institute of Science, Rehovot, Israel, in collaboration with Princeton University, Princeton, NJ and a B. S. in Life Sciences from Tel Aviv University, Tel Aviv, Israel. I hereby declare:

1. The extraction of isoflavones from soybeans is described in the attached article entitled "Ultrasound assisted extraction of soy isoflavones" (Rostagno, M.A. et al., Journal of Chromatography A, Volume 1012, Issue 2, 19 September 2003, Pages 119-128, attached hereto as Exhibit A). This article states as follows:

> Efficiency in extracting four isoflavone derivatives (daidzin, glycitin, genistin and malonyl genistin) from freeze dried ground soybeans was compared for mix-stirring extraction and ultrasound-assisted extraction, using different solvents and extraction temperatures with both. The efficiency of the extraction of soy isoflavones was improved by ultrasound but was dependent on the solvent employed. Optimization of the ratios of sample quantity to solvent volume and length of extraction time was also performed. ***Isoflavones can be quantitatively extracted from soybeans with 50% ethanol at 60°C using ultrasound-assisted extraction in 20 min.*** [Rostagno, et al., p. 119] (emphasis added)

Thus, I interpret from the Rostagno et al. publication that in order to extract acceptable levels of isoflavones from soybeans, a 50% ethanol solution should be used.

2. In another publication, titled "Improved methods for the extraction and analysis of isoflavones from soy-containing foods and nutritional supplements by reversed-phase high-performance liquid chromatography and liquid chromatography–mass spectrometry" (Aaron P. Griffith, Mark W. Collison, Journal of Chromatography A, 913 (2001) 397–413, attached hereto as Exhibit B), Section 3.5 states as follows:

> A relatively high concentration of organic solvent is required to extract all the forms of isoflavones and keep them in solution. Most previous isoflavone extraction methods either utilized 80% methanol as a solvent [3–7,15] or, after extracting in acidified water–acetonitrile mixtures, removed the solvent and dissolved the residue in 80% methanol [2,8,16,22,23]. In our laboratory, we found 60% acetonitrile was much better than 80% methanol for extracting isoflavones (Table 4). [Griffith et al., p. 404]

Table 5 of this publication indicates that a 10% solvent solution extracts very little in the way of isoflavones. As solvent concentration increases to about 50%, the yield of the extraction process is about 45-48%. Therefore, I conclude that the higher the percentage of solvent in the extraction solution, the higher the yield of the extraction process. Therefore, one of ordinary skill in the art at the time the invention described in the above-captioned patent application was made would have known that, in an isoflavone extraction process, it would have been preferred to use an extraction solution with a higher percentage of solvent, e.g., from about 50-60% solvent, rather than a very low percentage of solvent, e.g., less than about 10% solvent to extract isoflavones effectively.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dr. Miri Seiberg

Date